For the Love of Enzymes

THE ODYSSEY OF A BIOCHEMIST

Arthur Kornberg

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Foreword

Arthur Kornberg has played such a commanding role in the biochemistry of the gene that it is impossible to tell its history without including the personality that brought so much of that history about. For the Love of Enzymes combines personal memoir with scientific exposition—it is both an autobiography of a great scientist and a biography of the science to which he was devoted. This drama has little of the spice of interpersonal conflict, of any "race for the gold." Arthur Kornberg's rivalry has been with a reluctant Nature who demands ingenuity and perseverance before delivering the real prize, the secrets of how the world and its life are contrived.

My scientific acquaintances are almost evenly divided between those who were born with a passion for science, who have been driven by an inner vocation, and those who came to science as a later discovery, even an accident. Arthur Kornberg belongs to this second category; perhaps that explains the unflagging and methodical way in which he has pursued one accomplishment after another for four decades. The sense of balance and moderation he has brought to his professional life has allowed him to remain deeply devoted to his family, with no noticeable decrement to his scientific productivity. On the contrary, he has enjoyed not just companionship but also laboratory collaboration with a gifted wife (the late Sylvy Kornberg); and he has seen three sons exhibit extraordinary scientific and professional achievement. His talent and sensitivity as an administrator have built a department of biochemistry whose productivity is unmatched, and one which gives the lie to the proposition that science today is achievable only with immense groups and huge machines, or that it demands a renunciation of other human values.

Arthur's early life (like my own) typifies second-generation immigrant Jews in New York City, whose parents made great sacrifices to ensure an education for their children. Nothing in his home background pointed to science except the encouragement to study and to excel. The public schools reinforced that acculturation, by holding forth the ideal that academic achievement was the road of opportunity for social and economic mobility out of the sweatshops. City College in New York has nurtured a lion's pride of Nobel Prize winners, but it offered very little actual science in its undergraduate curriculum (and in those days none whatever at the graduate level). It did offer a talented, ambitious, and competitive peer group that helped to sharpen the aspirations of its students, and a faculty that, whatever else, fed the sense of individual worth of each of them, notwithstanding attributes of race, color, or economic class.

The world outside of City College was not so receptive; there were few opportunities open to Jews in academic or industrial science. The professions such as medicine (however the medical schools might ration their admissions) at least offered a prospect that individual careers might be built on ability rather than on membership in the right groups. A decade later, the mobilization of the universities to train young men and women in the skills needed during World War II finally cracked those ethnic barriers. Indirectly, the same process opened up the National Institute of Health, which gave Kornberg his first research opportunities.

I met Arthur Kornberg 35 years ago, at a summer course given by C. B. van Niel, where Arthur "learned microbiology" in preparation for taking that chair at Washington University. That fateful meeting led, five years later, to my appointment to Stanford University's department of genetics. I would indeed have preferred to be joining Arthur's new biochemistry department; but he and I have differences in how (or whether) we voice a philosophy of science that he may have been wise to foresee, even in our first meeting.

Kornberg's manifest approach to the choice of scientific problems is to focus on the particular, to eschew large social or scientific goals, to set aside grand design and theoretical synthesis. Every detail of enzymology is interesting to him; he says, "I have never met a dull enzyme." Yet, if not by design, then by intuition, Kornberg has always managed to sight the central targets of biological inquiry in his enzyme-hunting, and his method has consistently embraced far

broader issues than the mechanical steps of chemical purification and isolation.

Kornberg may be right that enzymology is daunting to many impatient youngsters and, lamentably, is being bypassed in favor of the more facile doctrines of gene hunting. I agree with him that the thousand-odd enzymes involved in intermediary metabolism and in the synthesis of nucleic acids and proteins are the fundamental periodic table of biology. As with the chemical atoms in Mendeleev's time, only a small proportion of the enzymes we can infer have actually been isolated; the arduous and indispensable task of isolating the rest must not be overlooked as the work of mapping the human genome commences in the next decade. But besides Kornberg's technical skills, we will need his knack for selecting those biochemical goals that warrant first priority. As he has always practiced, if not preached, we need to embed the knowledge of enzymes in a broader panoply of their functional relationships in the cell. This will require a host of other skills, like electron microscopy, MRI spectroscopy, and x-ray diffraction, not to mention genetic analysis. But the final test of our analytical methods is to reconstruct the cell, and for that we must have the purified components. Explanation in contemporary biology will continue to be chemistry. No one has taught us that lesson better than Arthur Kornberg.

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